

Please replace page 4, lines 1-13, of the specification with the following:

D³
--Four arginines replace according to the invention the B-domain of the FVIII protein. They are introduced by the oligonucleotides used for the cloning of the two fragments surrounding the B-domain (see Fragments 2 and 3 of Table 1), namely the oligonucleotides 4R AS (SEQ. ID No. 4) and 4R S (SEQ. ID No. 5). The Sal I site was generated by the coding sequence of the arginines as follows:

SAL I SITE

4R S :5'-A AGA CGT CGA CGA GAA ATA ACT CGT ACT ACT CTT (SEQ. ID No. 5)

4R AS TTG TTA CGG TAA CTT GGT TCT GCA GCT GCT CTT (SEQ. ID No. 4)

CORRESPONDING PEPTIDIC SEQUENCE:

Pro Arg Arg Arg Arg Glu Ile Thr Arg Thr Thr Leu (SEQ. ID No. 12)

In the wild-type FVIII the peptidic sequence is:

Pro-Arg-Domain B-Arg-Glu --

Please replace page 6, lines 1 through 5, of the specification with the following:

D⁴
--The FIX T11 sequence (SEQ. ID No. 9) used according to the invention in different locations of the FVIII cDNA starts after the coding sequence by the splice donor sequence and ends by the splice acceptor sequence of the truncated intron 1. The upper case letters start after and stop before the Nsi I and Mlu I restriction sites, respectively. For details, see Annex 2. --

Please add Annex 2 to the specification, following the sequence listing:

Annex 2

Oligonucleotides used for introducing TFIXI1 in FVIII sequence

The oligonucleotide sense is always presented first.

Oligonucleotides used for introducing two restriction sites in TFIXI1:

FVIII IB-S: 5'- C AT GCA T CC TTT TTT AAA ATA CAT TGA G (SEQ. ID No. 14)

Nsi I site

FVIIB-AS: 5'- A AC GCG T TA ATT CTT TAG TTT TAG CA (SEQ. ID No. 15)

Mlu I site

**Oligonucleotides used for the generation of FVIII compatible ends to clone in
FVIII intron 1 location**

-Generation of I1 A

FVIII ATG: 5'-ACA CCC ATG GAA ATA GAG CTC TCC ACC TGC (SEQ. ID No. 1)

FVIII IA-AS: 5'-A AT GCA T (AA ACA AAC) CTT GCG TCC ACA GGC AGC TC (SEQ.

ID No. 16) **Nsi I site** FIX splice donor

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

-Generation of I1 B

FVIII IC-S: 5'-A **AC GCG T** (AT TCT TTT ACA TTT CAG) ATT TCC TCC TAG AGT

GCC (SEQ. ID No. 17) **Mlu I site** FIX splice donor

AAA ATCT

FVIII 585-AS: 5'-TTC TCT ACA T **AC TAG T** AG GGC (SEQ. ID No. 18)

endogenous FVII Spel site

Oligonucleotides used for the generation of FVIII compatible ends to clone in FVIII

intron 12 location

-Generation of I12A

5' Bgl II: 5'-AAT ATG GAG AGA GAT CTA GCT TCA GG (SEQ. ID No. 3)

FVIII 12-AS: 5'-A **AT GCA T** (AA ACA AAC) TGT GCA TGA TGT TGG AGG CT (SEQ.

ID No. 19) **Nsi I site** FIX splice donor

-Generation of I12C

FVIII 12C-S: 5'-A **AC GCG T** (AT TCT TTT ACA TTT CAG) GCA TCA ATG GCT ATG

TTT (SEQ. ID No. 20) **Mlu I site** FIX splice acceptor sequence

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com